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HLA-typing in Schistosoma Japonicum infection

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tion medium was used throughout, the discrepancies which occurred between the various plates can only be due to one, or more, of three factors: (a) deterioration in the standard stock solutions of chloroquine phosphate used for dosing the plates; (b) errors in the preparation of the serial dilutions of chloroquine phosphate used in dosing the plates; or (c) deterioration of the chloroquine phosphate after dosing the plate.

Concerning the first possibility, the stock solutions are specially prepared and quality-controlled in a pharmaceutical industry laboratory of impeccable reputation. In longitudinal studies the stock solutions have been shown to be absolutely stable over *three* years of shelf-life.

Concerning the second possibility, serial dilutions are always made by 2 persons using a standard written protocol, the second person monitoring the actions of the first. Thus the possibility of error is extremely small. Such error would be evident throughout the particular batch and detected through external quality control.

Finally, since the quantity of the drug deposited in the test plate well is extremely small (the highest concentration of the plates under discussion is only 32 pmol/well), deterioration can be expected over time and is known to be enhanced by high ambient temperatures.

Control plates stored at ambient temperature in closed cupboards at WHO headquarters in Geneva have uniformly demonstrated a minimum shelf-life of *two* years. Similarly, control test plates stored under normal refrigeration in the tropics (Thailand) have shown a similar shelf-life without deterioration. Studies to date indicate that changes do occur at about 3 years even under ideal storage conditions.

From the evidence made available by S. Sinha and A. Gajanana we can only conclude, therefore, that the deterioration they note was probably due to inappropriate storage of the plates and we would like to take this opportunity to impress upon our collaborators who use these plates the importance of proper storage and handling, a point which is stressed in the instructions accompanying the microtest kit.

On a point of technique, we noticed that S. Sinha and A. Gajanana used the MIC as the crucial criterion. Log dose/response regression data were unfortunately not available. Very low schizont counts, as are common at drug concentrations near the threshold level, increase the probability of missing schizonts. The MIC is therefore subject to considerable statistical error and is probably not the ideal quantity for measuring interplate or intraplate variation. Given adequate sample size, an effective concentration (EC) value between EC_{16} and EC_{84}, e.g. EC_{50}, would probably better reflect such variation.

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HLA-typing in *Schistosoma japonicum* infection

We were very interested to read about HLA typing in patients with differing clinical manifestations of *Schistosoma japonicum* infection in Leyte, Philippines (Ohta *et al.*, 1987: *Transactions*, **81**, 292). We have also wondered why patients seem to have either cerebral or hepatic involvement, but not both, and recently performed HLA typing on 41 schistosomiasis patients and 25 uninfected Filipino controls in an attempt to explore a possible genetic explanation for this phenomenon. Unlike Ohta *et al.*, we observed HLA-B16 in hepatosplenic patients (Table). HLA-B40 was found in both groups. Neither these nor any other HLA-types, either singly or in combination, were significantly more frequent in patients with cerebral schistosomiasis than in patients with hepatosplenic disease or uninfected controls. However, the number of cerebral patients was small because only proven cases were studied.

Table—Prevalence of 2 HLA-antigens in patients with cerebral and hepatosplenic schistosomiasis

	Cerebral (n = 6)	Hepatosplenic (n = 35)	Controls (n = 25)
HLA-B16	1 (17%)	9 (26%)	6 (24%)
HLA-B40	3 (50%)	16 (46%)	14 (56%)

We agree that it is particularly important to investigate the HLA-D region antigens with regard to disease associations (Tiwari & Terasaki, 1981: In: *The Lymphocyte*, New York: Alan R Liss, Inc., pp. 151-163) and look forward to learning the results of further studies by Ohta *et al.* However, we hope that Filipino patients without schistosomiasis will serve as controls rather than the Japanese controls used for the Leyte study. It is also important that cerebral schistosomiasis be carefully defined. In some endemic areas, virtually everyone is infected so that seizures may be associated with, but not due to, schistosomiasis. 64% of patients with schistosomiasis and acquired seizures in our recent study were found to have central nervous system disease unrelated to *S. japonicum* infection (Watt *et al.*, 1986: *Lancet*, ii, 529). Computerized tomography appears to be the most valuable tool for establishing cerebral schistosomiasis as the cause of seizures.

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Treatment of the acute (toxaemic) phase of schistosomiasis with oxamniquine

In a recent review of clinical experience with oxamniquine, Foster (1987: *Transactions*, **81**, 55) presented some data on the treatment of the acute (toxaemic) phase of schistosomiasis that could confuse readers not familiar with the difficulties of treatment of this serum sickness-like disease.

Foster wrote: "A cure rate of 93% was recorded in 15 patients in the acute (toxaemic) phase of the

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HLA-typing was recently performed on 41 schistosomiasis patients and 25 uninfected Filipino controls to investigate why patients have either cerebral or hepatic involvement. Neither the following tests HLA-B16, HLA-B40, nor other HLA-typing were significantly frequent in patients with cerebral schistosomiasis. Keywords: Biology; diagnostic medicine

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